DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

9/864d

OCT - 4 2001

WARNING LETTER

Food and Drug Administration
Rockville MD 20857

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Reference No. 01-HFD-45-0402

Barry S. Levine, D.Sc.
Laboratory Director
Toxicology Research Laboratory
University of Illinois at Chicago
Department of Pharmacology
1940 W. Taylor St.
Chicago, IL 60612-7353

Dear Dr. Levine:

During January and February of 2001, an investigator from the Food and Drug Administration's (FDA) Chicago District Office inspected the following studies conducted in your nonclinical laboratory facility:

Study #323: "Six Month Oral Toxicity Study of [redacted] with a One Month Recovery Period in Dogs"
Study #224: "Oral Prenatal and Postnatal Development Study of [redacted] in Rats"

This inspection was conducted as part of the FDA's Bioresearch Monitoring Program, which includes inspections to monitor the conduct of research involving investigational new drugs.

During the inspection, our investigator observed a number of deviations from the Good Laboratory Practice (GLP) regulations. The deficiencies were listed on Form FDA 483 (copy enclosed), which was presented to you and discussed at the conclusion of the inspection.

Following review of the Form FDA 483, the inspection report, and data collected during the inspection, the Division of Scientific Investigations concludes that there were serious violations of the GLP regulations, Title 21 CFR, Part 58:

(1) You failed to assure that the test articles and dosing formulations for studies #224 and #323 were appropriately tested for identity, strength, and stability. (21 CFR 58.31(d)) Different methods were used for initial and periodic testing, and records were incomplete and/or unavailable for method validation, chromatograms, mass spectra, and sources and amounts of reference materials used for calibration.

(2) You failed to describe completely, in the final study report for study #323, relevant dosing issues and other circumstances that may have affected the quality or integrity of the data. (21 CFR 58.185(a)(8-9)) The final report failed to completely describe the observations of Giardia infection, diarrhea during the quarantine period, vomiting and redosing of capsules for five months of the study, and their consequences to systemic absorption of [ ]

(3) Finally, the testing facility management failed to promptly replace the study director for studies #323, 340, 345, and 354 after the departure of the original study director. (21 CFR 58.31) As a result, you failed to assure that protocol deviations and QAU inspection reports for study #323 were evaluated by a replacement study director.

The above description of violations is not intended to be an all-inclusive list of deficiencies at your facility. Please note that failure to correct these violations may result in regulatory action without further notice.

You should notify this office in writing, within fifteen (15) working days of receipt of this letter, with specific steps you have taken to bring your facility into compliance with FDA's regulations.

If you have any questions, please contact:

C.T. Viswanathan, Ph.D.
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Chief, GLP and Bioequivalence Investigations Branch
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place, Room 151
Rockville, Maryland 20855
Telephone: (301) 827-5460

Sincerely,

Joanne L. Rhoads M.D.

Joanne L. Rhoads, M.D., M.P.H.
Acting Director
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research

Enclosure: Form FDA 483